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Title: Dosimetric advantage of intensity-modulated radiotherapy for whole ventricles in the treatment of localized intracranial germinoma

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Katsuyuki Sakanaka, none; Takashi Mizowaki, none; Masahiro Hiraoka has a contract of sponsored research program with Varian Medical Systems.

Abstract

Purpose: To investigate the dosimetric advantage of intensity-modulated radiotherapy (IMRT) for whole ventricles (WV) in patients with a localized intracranial germinoma receiving induction chemotherapy. **Methods and Materials**: Data from 12 consecutive patients with localized intracranial germinomas who received induction chemotherapy and radiotherapy were used. Four-field coplanar three-dimensional conformal radiotherapy (3DCRT) and seven-field coplanar IMRT plans were created. In both plans, 24 Gy was prescribed in 12 fractions for the planning target volume (PTV) involving WV and tumor bed. In IMRT planning, optimization was conducted to reduce the doses to the organs at risk (OARs) as much as possible, keeping the minimum dose equivalent to that of 3DCRT. The 3DCRT and IMRT plans were compared in terms of the dose-volume statistics for target coverage and the OARs. **Results**: IMRT significantly increased the percentage volume of the PTV receiving 24 Gy compared with 3DCRT (93.5% vs. 84. 8%; $p = 0.007$), while keeping target homogeneity equivalent to 3DCRT ($p = 0.869$). The absolute percentage reduction in the irradiated volume of the normal brain receiving 100%, 75%, 50%, and 25% of 24 Gy ranged from 0.7% to 16.0% in IMRT compared with 3DCRT ($p < 0.001$). No significant difference was observed in the volume of the normal brain receiving 10% and 5% of 24 Gy between IMRT and 3DCRT. Conformation number

was significantly improved in IMRT ($p < 0.001$). For other OARs, the mean dose to the cochlea was reduced significantly in IMRT by 22.3% of 24 Gy compared to 3DCRT ($p < 0.001$). **Conclusions**: Compared with 3DCRT, IMRT for WV improved the target coverage and reduced the irradiated volume of the normal brain in patients with intracranial germinomas receiving induction chemotherapy. IMRT for WV with induction chemotherapy could reduce the late side effects due to cranial irradiation without compromising control of the tumor.

Keywords: Germinoma; Whole ventricular radiotherapy; Radiotherapy, Intensity-Modulated; Planning study

Introduction

Radiotherapy is an effective treatment modality in the treatment of intracranial germinomas (1). Craniospinal plus boost radiotherapy has achieved high survival rates of more than 90% at 10 years (2–4). The achievement of the high survival rate in young patients raised the concerns to the potential late side effects of the craniospinal radiotherapy such as cognitive impairment, endocrine dysfunction, secondary tumors, and occlusion of brain arteries in long-term survivors (5, 6). To resolve them, the dose-reduced or irradiated volume-reduced radiotherapy for intracranial germinoma have been attempted. In contrast to the poor disease control by small local field radiotherapy or intensive chemotherapy alone (7, 8), the radiotherapy involving whole ventricles (WV) could reduce the irradiated volume of the brain without compromising disease control. The reported overall survival rate was 93.7–100% at 5 years (9, 10) and 91–92% at 10 years (11, 12). Three-dimensional conformal radiotherapy (3DCRT) for WV could be an alternative treatment to craniospinal plus boost radiotherapy in the treatment of localized intracranial germinomas.

The shape of WV is too complex for 3DCRT to deliver a conformal dose to the WV. High dose exposure to the brain surrounding the WV was unavoidable in 3DCRT technique. Unlike 3DCRT, intensity-modulated radiotherapy (IMRT) could deliver a

conformal dose to the target volume and spare organs at risk (OARs). The dosimetric advantage of IMRT for WV has been investigated by other researchers (13, 14). The focused point in their reports was the reduction of the dose to the brain. The effect of IMRT on the dose distribution in target was not examined. The effect of IMRT on the target coverage is another important issue in the planning study of IMRT because adequate dose coverage to WV is indispensable to achieve disease-free rates comparable to those of craniospinal radiotherapy (8, 15). It remains unclear whether both an improvement in target coverage and OAR-sparing are achievable in IMRT for WV.

This study included the data of 12 patients suffering from localized intracranial germinomas who were treated with radiotherapy after induction chemotherapy in our hospital. To evaluate the dosimetric advantages of IMRT for WV, we excluded boost radiotherapy from this planning study and compared the plans of 3DCRT and IMRT for the WV using dose-volume indices of target coverage and OARs. The aim of this study was to determine whether IMRT to the WV can improve target coverage and spare OARs in patients with localized intracranial germinomas who have received induction chemotherapy, compared with 3DCRT for WV.

Materials and Methods

Eligibility criteria

Twelve patients underwent radiotherapy following induction chemotherapy for localized intracranial germinoma at Kyoto University Hospital between June 2003 and March 2010. The mean age was 18.2 (range 5–34) years. The primary sites included five suprasellar lesions, four pineal lesions, and three combined pineal and suprasellar lesions. All patients were given two or three courses of platinum-based induction chemotherapy. Complete remission was confirmed by magnetic resonance imaging (MRI) in all patients, before computed tomography (CT) was performed. During the CT simulation study, all patients were placed in the supine position with the head tilted forward and immobilized with a thermoplastic mask. CT with intravenous contrast material was performed with a 2.5-mm slice thickness using a LightSpeed RT (General Electric Medical Systems).

Volume definition

The CT images were exported into the Eclipse treatment planning system (ver. 8.6; Varian Medical Systems). In this study, the clinical target volume (CTV) was defined as the volume of the tumor bed before induction chemotherapy with a 15-mm margin and the third, fourth, and lateral ventricles with a 5-mm margin. The tumor bed was contoured on the each slice of the CT images, referring to the MRI taken before induction

chemotherapy. The third, fourth, and lateral ventricles were contoured using MRI taken between completion of the induction chemotherapy and the CT simulation. The volumes of organs at risk (OAR), *i.e.*, the brain, chiasm, optic nerves, lens, pituitary gland, and cochlea, were also contoured. The report by Merchant *et al*. was referred to when defining the volume of the cochlea (16). Two radiation oncologists (KS and TM) confirmed the contoured volumes. The volume of the tumor bed in the suprasellar region was non-uniformly enlarged to exclude bone and sinuses from the CTV. The planning target volume (PTV) was defined as an additional 5-mm margin around the CTV. The mean volumes of the tumor bed, WV, PTV, and normal brain, which was defined as the volume of the brain outside the PTV, were 3.6 (range 0.1–15.6), 50.7 (range 33.3–84), 364.4 (range 295.7–425.0), and 1058.2 (range 759.3–1210.3) mL, respectively. The patient characteristics are summarized in Table 1.

Treatment planning

All treatment plans were created using 6 MV photon beams from a Varian CL21iX linear accelerator and Millennium 120-leaf multileaf collimator (Varian Medical Systems). Pencil beam convolution was used for dose calculation, with a 2.5-mm grid size.

The 3DCRT plans were created with a pair of the coplanar anteroposterior and opposed lateral beams centered on the PTV. The PTV was encompassed by irradiation fields with 5-mm jaw and leaf margins. In total, 24 Gy in 12 fractions was prescribed to the isocenter of the irradiation fields, except for two patients, in whom the isocenter dose was reduced so that the maximum dose was less than 107% of the prescribed dose in the irradiated volumes.

In IMRT planning, seven-field coplanar beams were used with fixed gantry angles of 0, 55, 105, 155, 205, 255, and 305° using the same isocenter position for the planned 3DCRT. The Eclipse fluence-based algorithm (Varian) was used in the optimization method. Multileaf collimator leaf sequences were generated using the dynamic sliding window technique. The planning goals of IMRT were to reduce the doses to the OARs, to below the doses seen with 3DCRT, while keeping the minimum target coverage equivalent to that planned with 3DCRT (Table 2). We defined the dose encompassing 99% of the PTV volume (D99%) as a surrogate index for the minimum dose to the PTV. Optimization was conducted as follows: the maximum dose (D_{max}) to the PTV was reduced to less than 107% of the prescribed dose, keeping the equivalent D99% to the PTV in 3DCRT. D_{max} to the normal brain and the irradiated volume of the normal brain were reduced as far as the optimization did not ruin the target coverage. The dose

reduction to the OARs other than to the normal brain was a lower priority than the target coverage and the normal brain sparing in the optimization.

Assessment of endpoints

The dose indices used to compare 3DCRT with IMRT were selected by referring to the recommendations for documenting IMRT treatments by the American Society for Radiation Oncology workgroup (17). To evaluate the target coverage, D_{max}, the dose covering 1% of the structure volume (D1%), mean dose (D_{mean}), the dose that covers 95% of the structure volume (D95%), minimum dose (D_{min}), and homogeneity index (HI = D_{max}/D_{min}) were used. The doses to the normal brain were assessed using D_{max}, D1%, and D_{mean}. The irradiated volume of the normal brain was evaluated using the percentages of the volume of the normal brain receiving 100, 75, 50, 25, 10, and 5% of the prescribed dose (V100%, V75%, V50%, V25%, V10%, and V5%, respectively). The conformation number (CN) in plans of 3DCRT and IMRT was calculated. CN was defined as follows; $CN = (TV_{RI}/TV) \times (TV_{RI}/V_{RI})$ where TV_{RI} = target volume covered by the reference isodose, TV = target volume and V_{RI} = the volume of the reference isodose (18). 95% isodose was used for the reference isodose. The CN ranges from 0 to 1, where 1 is ideal value and 0 is least. The doses to the OARs were evaluated using D_{max} and D_{mean}.

Statistical analyses

The paired *t*-test was used to compare the dose-volume indices of the PTV and OARs between 3DCRT and IMRT. All statistical tests were two sided and a *p* value of less than 0.05 was considered to indicate statistical significance. The statistical analyses were conducted using GraphPad Prism (ver. 5.03; GraphPad Software).

Results

The CT images showing the dose distributions of 3DCRT and IMRT for a representative patient are shown in Figure 1.

PTV coverage

The mean D99% to the PTV was 97.8% of the prescribed dose (range 95.8–99.0) in all plans. V100% of the PTV was significantly higher in IMRT than that in 3DCRT (93.5% vs. 84.8%; $p = 0.007$). No significant difference was observed in HI, D_{min} to the PTV, or D_{max} to the PTV between 3DCRT and IMRT ($p = 0.869$, 0.616, and 0.058, respectively). D1%, D95%, and D_{mean} to the PTV were significantly higher in IMRT than in 3DCRT ($p = 0.012$, <0.001, and 0.002, respectively). The absolute differences in D1%, D95%, and D_{mean} between 3DCRT and IMRT were from 0.7% to 1.4% of the prescribed dose (Table 3). Figure 2(a) shows the mean dose-volume histogram (DVH) of the PTV. The mean DVH in 3DCRT had a relatively wider shoulder for the PTV than that seen in IMRT.

Sparing the volume of the normal brain and the OARs

D1% and D_{mean} to the normal brain were significantly lower in IMRT than in 3DCRT by 1.8% and 6.0% of the prescribed dose, respectively ($p < 0.001$; Table 3). The irradiated volume of the normal brain was reduced throughout the low-to-high dose areas

in the mean DVH of the normal brain (Figure 2(b)). V100%, V75%, V50%, and V25% of the normal brain were reduced significantly in IMRT versus 3DCRT (4.9% vs. 20.9%, 36.2% vs. 47.3%, 73.0% vs. 80.0%, and 85.0% vs. 85.7%, respectively; all $p < 0.001$). No significant difference was observed in V10% or V5% of the normal brain between IMRT and 3DCRT (93.8% vs. 93.9%, 89.7% vs. 89.9%; $p = 0.901$ and 0.284, respectively). The CN was smaller in 3DCRT than IMRT (0.48 vs. 0.70; $p < 0.001$). D_{max} and D_{mean} to the cochlea were significantly lower in IMRT than in 3DCRT, by 7.9% and 22.3% of the prescribed dose, respectively. For the other OARs, small differences were observed between 3DCRT and IMRT, from 0.6 to 4.9% of the prescribed dose (Table 4). The mean monitor units to deliver a 2.0-Gy fraction were 249 (range 240–254) in 3DCRT and 980 (range 806–1149) in IMRT.

Discussion

We found that compared with 3DCRT, IMRT for WV improved the target coverage and reduced the dose to the normal brain and cochlea in patients with localized intracranial germinomas receiving induction chemotherapy. Only small differences were observed for doses distributed to other OARs. As expected, a larger number of monitor units was needed in the plans for IMRT.

Comparison with the reported target coverage

In this study, V100% of the PTV was higher in IMRT than in 3DCRT, while keeping the equivalent minimum dose coverage and homogeneity seen in 3DCRT. Previous planning studies of IMRT for WV (Table 5), emphasized the dosimetric advantage, such as the reduction of the irradiated brain volume, but did not examine the dosimetric influences on target coverage (13, 14). Based on our literature search, ours is the first reported planning study to indicate that IMRT for WV improves target coverage and spares OARs.

IMRT spares OARs, but may reduce target homogeneity as a trade-off (19, 20). This means that IMRT delivers lower minimum and higher maximum doses to the target than 3DCRT. In dose- and volume-reduced radiotherapy for intracranial germinomas, a lower minimum dose to WV is undesirable because inadequate doses delivered area in

WV result in a higher rate of regional recurrence (8, 15). In the study of recurrence pattern in 60 patients with intracranial germinoma who received chemotherapy with limited field radiotherapy, most of the recurrences were observed in inadequately dose-delivered ventricular area (8 of 10 patients). Five patients experienced a recurrence in the presumably 20–36 Gy delivered region of cerebral ventricles (21). In addition to the lower minimum dose to the PTV, special consideration may be required for the maximum dose to the PTV, because most of the PTV consisted of the volume of the brain after induction chemotherapy. The volume of the brain within the PTV ends up receiving a higher dose even if IMRT spares the normal brain outside the PTV. For IMRT planning, the homogenous dose distribution is both favorable and safer by avoiding unexpected side effects to the normal brain. D1% to the PTV was significantly higher in IMRT planning than those seen in 3DCRT, but it was a small difference (0.7% of the prescribed dose). We believe that the improvement in V100% of the PTV and the normal brain sparing were more advantageous clinically than the disadvantage caused by the small increase of D1% in the radiotherapy of intracranial germinoma.

Comparison with reported brain sparing

Planning studies for IMRT for WV focusing on brain sparing have been reported in the treatment of intracranial germinomas. IMRT for WV reduced both the D_{mean} to the

brain and the brain volume that received the high dose. However, the reported dose-volume histograms showed that there was an increase in the low-dose irradiated brain volume (13, 14). Chen *et al*. reported that IMRT for WV could reduce the irradiated volume of the cerebral hemisphere, even at a low dose (22). They compared IMRT plans used clinically with the best 3DCRT plans in the treatment of intracranial germ cell tumors. In radiotherapy for intracranial germ cell tumors other than intracranial germinomas, boost radiotherapy for the primary lesion was indispensable, in addition to radiotherapy for the whole central nervous system, whole brain, or WV (23, 24). The study by Chen *et al*. enrolled patients with intracranial germ cell tumors and their planning study included boost radiotherapy. In this study, we focused on the dosimetric advantage of IMRT for WV in the treatment of intracranial germinomas, which is the most common subset of intracranial germ cell tumors (25). In contrast to the other intracranial germ cell tumors, WV radiotherapy without a boost was one of the best treatment options that could result in a cure (9). Our study showed that IMRT for WV reduced the irradiated volume of the normal brain that received high-to-low dose exposure, while achieving target coverage in the treatment of intracranial germinomas equivalent to that with 3DCRT. Clinically, the reduction in the volume of the irradiated

normal brain can be useful for preserving cognitive function and is not harmful if salvage radiotherapy is needed.

Comparison with reported doses to OARs

In this study, D_{mean} to the cochlea was reduced by 22.3% of the prescribed dose in IMRT planning compared with that in 3DCRT. A prospective study reported that a dose to the cochlea of 35 Gy affected the patient's hearing (26). The threshold of cochlea damage from irradiation was lowered through a combination of platinum analogs (27). The dosimetric advantage of sparing the cochlea using 3DCRT or IMRT was shown in studies of brain tumor radiotherapy, and was beneficial in reducing hearing deterioration (16, 28). In radiotherapy for WV, the cochlea was outside the PTV in all of our patients and the dose to the cochlea was reduced in IMRT planning without compromising target coverage. We expect that the reduced dose to the cochlea in WV radiotherapy would help to spare the hearing of patients with localized intracranial germinomas.

Raggi *et al*. reported pituitary gland sparing through a mean reduction of 1 Gy in IMRT planning. A dose reduction to the suprasellar region is desirable to maintain the function of the hypothalamic-pituitary axis (29). However, the volume of the hypothalamus and pituitary gland was included in the PTV in all plans in our study, especially when the primary lesion was located in the suprasellar region. Adequate dose

delivery to the WV is indispensable for controlling intracranial germinomas (8, 15). In our study, dose reduction to the pituitary gland was not prioritized in the optimization process. The differences in the doses to the optic nerve, chiasm, and lens between IMRT and 3DCRT were small (Table 4) and may be irrelevant clinically.

Increase in monitor units and associated problems

Leakage and scattered beams are two important issues in IMRT treatment. To perform IMRT, the linear accelerator must be energized for a longer time and more monitor units are needed, compared with 3DCRT, when delivering the same dose (30). Hall *et al*. reported that IMRT may increase the incidence of solid cancers because more monitor units result in higher total-body low-dose exposure (31, 32). However, Tubiana *et al*. pointed out that the recent biological data were not compatible with “linear no threshold” (LNT) relationships and the LNT dose-effect relationship led to an overestimation of the carcinogenesis risk of low doses (33, 34). One cohort study of secondary solid tumors after radiotherapy indicated that 78% of secondary malignancies arose in the central PTV or surrounding area (35). Our results showed that IMRT spares the normal brain near the PTV without increasing the low-dose irradiated volume of the normal brain. Regarding the issue of secondary malignancies, we believe that the benefits

of sparing the volume of the normal brain receiving high doses by using the IMRT technique outweigh the disadvantages due to leakage and scattered radiation.

Limitations of this study

This study included the 12 consecutive patients with intracranial germinomas who were treated in our hospital. Intracranial germinomas are rare tumors (25). If more samples were included in this study, statistically significant differences might have be observed regarding D_{max} to the PTV and D_{max} to the normal brain, although the observed differences were less than 1.0% of the prescribed dose. The effects on the clinical outcomes resulting from these differences may be relatively small, considering the contributions of the improved target coverage and sparing of the normal brain.

In conclusion, IMRT for WV improved target coverage and reduced the irradiated volumes of normal brain and the dose to the cochlea compared with 3DCRT without increasing low-dose exposure to the normal brain. IMRT for WV could improve local tumor control and reduce concerns regarding late side effects resulting from cranial irradiation in patients with intracranial germinoma. Our results may facilitate the use of IMRT for WV in the treatment of intracranial germinomas.

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Figure legends

Figure 1. Multi-plane slices showing the isodose distributions for (a) four-field coplanar three-dimensional conformal radiotherapy and (b) seven-field coplanar intensity-modulated radiotherapy. Yellow contour = tumor bed before induction chemotherapy; blue contour = whole ventricles; green contour = clinical target volume; red contour = planning target volume.

Figure 2. Mean cumulative dose-volume histograms for (a) PTV and (b) normal brain for 3DCRT and IMRT.

Abbreviations: PTV = planning target volume; normal brain = the volume of the brain outside the PTV; 3DCRT = four-field coplanar three-dimensional conformal radiotherapy; IMRT = seven-field coplanar intensity-modulated radiotherapy.

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Fig. 1(a)

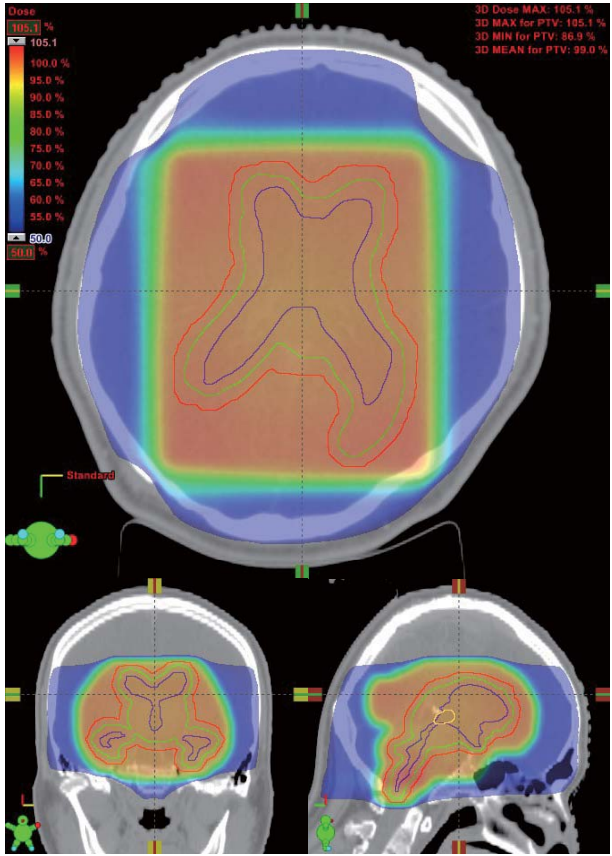
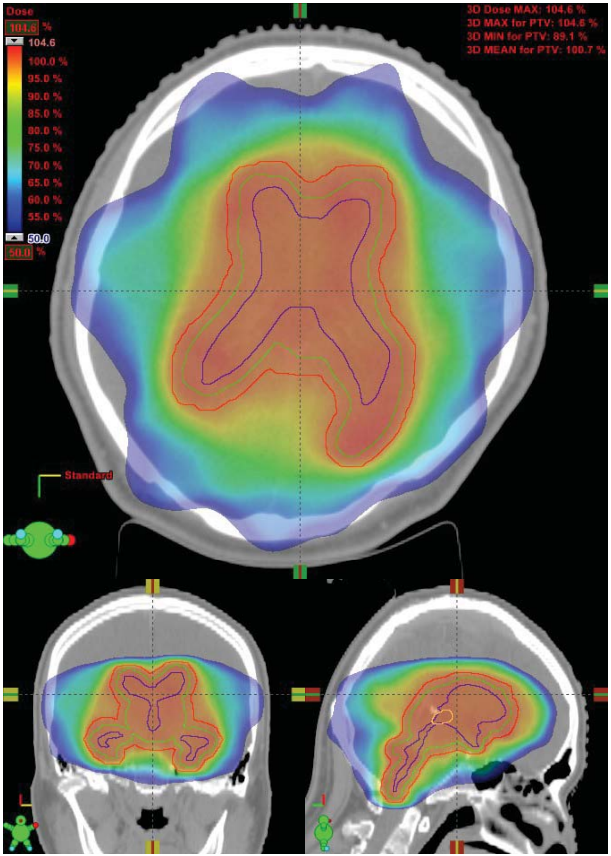
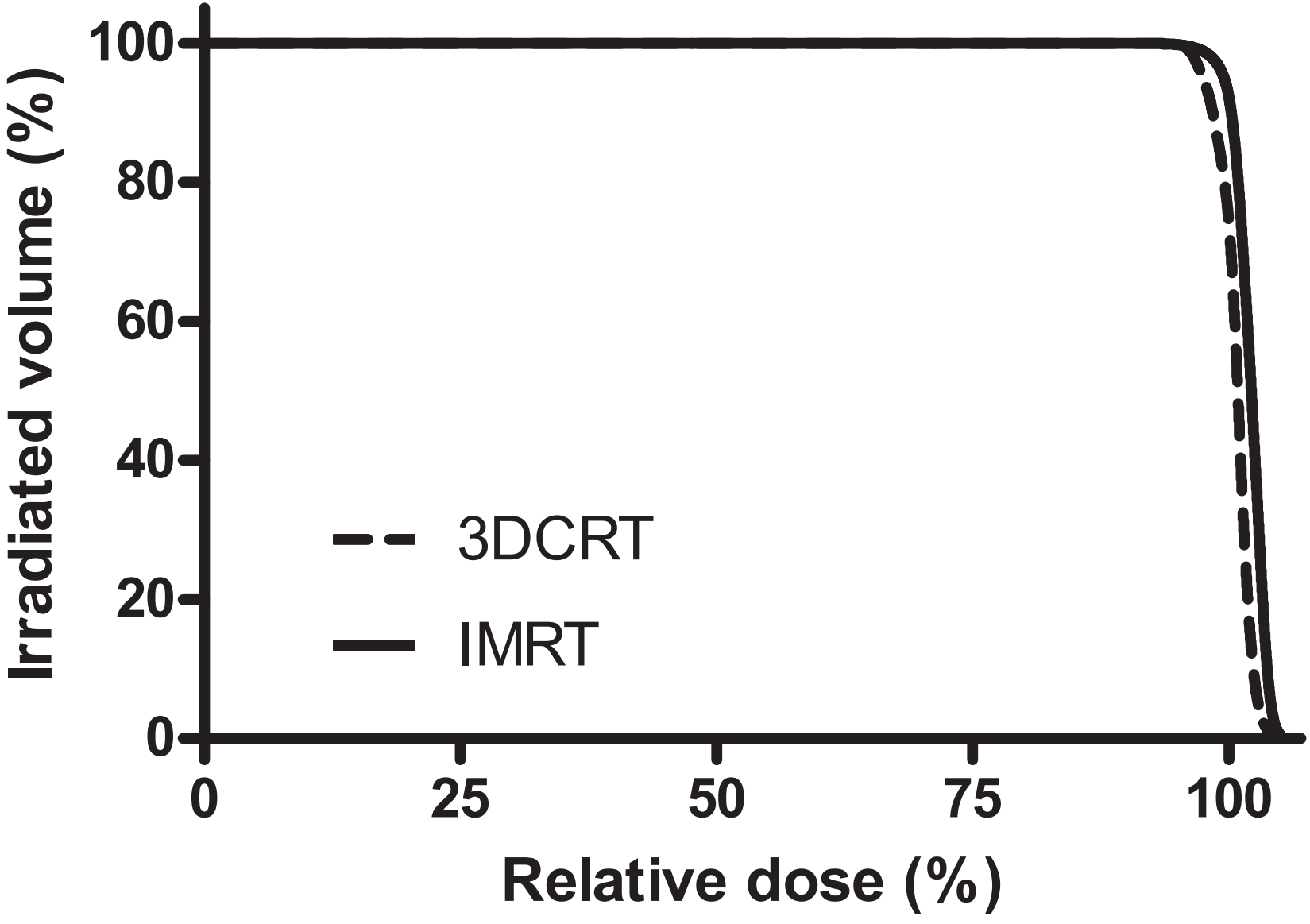
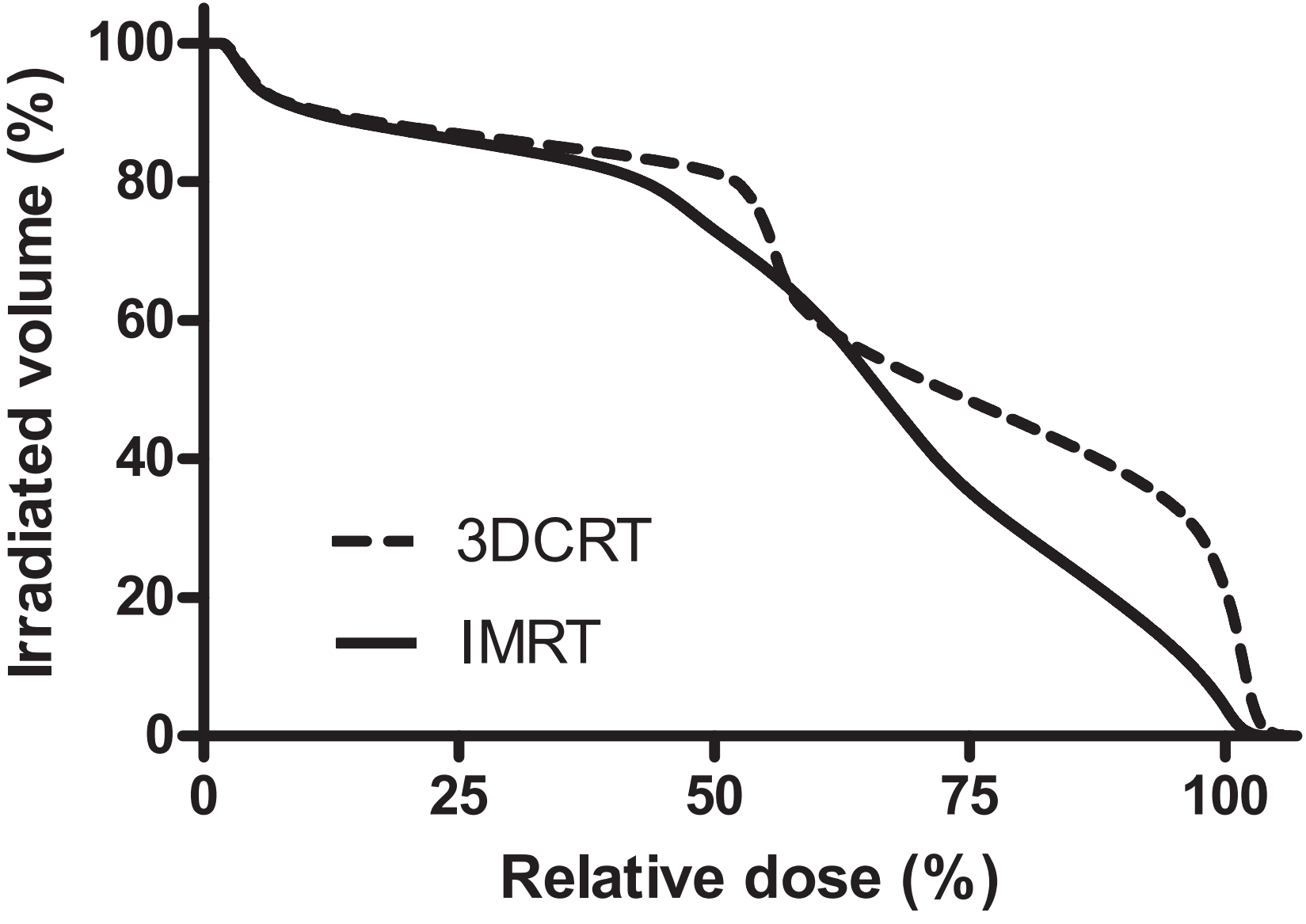


Fig. 1(b)







Tables

Table 1. Patient characteristics and tumor status

Gender	
M	9
F	3
Age (years)	18.2 (range 5–34)
Primary site	
Pineal region	4
Suprasellar region	5
Bifocal region	3
Tumor bed (mL)	3.6 (range 0.1–15.6)
Ventricles (mL)	50.7 (range 33.3–84)
PTV (mL)	364.4 (range 295.7–425.0)
Normal brain (mL)	1058.2 (range 759.3–1210.3)

Abbreviations: PTV = planning target volume; normal brain = the volume of the brain outside the PTV.

Table 2. Optimization workflow

Step 1	
Reduce the dose to normal brain, keeping the equivalent minimal dose to the PTV	
Constraints of PTV	
Minimum dose	Achieve the equivalent D99% to the PTV in 3DCRT plans
Maximum dose	Reduce D_{max} to the PTV as much as possible, to at least less than 107% of the prescribed dose
Constraints of brain	
Reduce D_{max} to the normal brain and the irradiated volume of the normal brain as much as possible, while satisfying the constraints of the PTV	
Step 2	
Reduce the dose to OARs, keeping the constraints of the PTV and normal brain in Step 1	

Abbreviations: normal brain = the volume of the brain outside the planning target volume; PTV = planning target volume; D99% = the dose that covers 99% of the structure; D_{max} = the maximum dose to the structure volume; OARs = organs at risk.

Table 3. Summary of dose-volume histogram analysis of PTV and normal brain: mean value (range)

	3DCRT	IMRT	Difference	*p* value
PTV				
D_{max} (%)	105.0 (103.3–107.0)	105.7 (104.6–107.0)	+0.7	0.058
D1% (%)	103.6 (102.0–105.0)	104.3 (103.3–105.9)	+0.7	0.012
D_{mean} (%)	100.7 (98.3–101.6)	102.1 (100.7–104.0)	+1.4	0.002
D95% (%)	99.1 (96.6–100.2)	100.0 (98.3–101.6)	+0.9	< 0.001
D_{min} (%)	89.6 (85.8–94.1)	89.9 (85.7–93.2)	+0.3	0.616
V100% (%)	84.8 (64.4–96.2)	93.5 (78.0–98.0)	+8.7	0.007
HI (%)	1.17 (1.12–1.23)	1.17 (1.13–1.23)	0.0	0.869
Normal brain				
D_{max} (%)	105.1 (103.9–106.3)	104.4 (102.7–105.7)	–0.7	0.065
D1% (%)	103.3 (100.8–104.9)	101.5 (99.47–103.5)	–1.8	< 0.001
D_{mean} (%)	68.2 (61.20–75.40)	62.2 (55.90–70.00)	–6.0	< 0.001
Conformation number	0.48 (0.43–0.55)	0.70 (0.60–0.76)	+0.22	< 0.001

Abbreviations: PTV = planning target volume; normal brain = the volume of brain outside the PTV; 3DCRT = four-field coplanar three-dimensional conformal radiotherapy; IMRT = seven-field coplanar intensity-modulated radiotherapy; D_{max} = the maximum dose to the

structure; D1% = the dose that covers 1% of the structure volume; D_{mean} = the mean dose to the structure; D95% = the dose that covers 95% of the structure volume; D_{min} = the minimum dose to the structure; V100% = the percentage of the structure volume receiving the prescribed dose; HI = homogeneity index (D_{max}/D_{min}); Conformation number = $(TV_{RI}/TV) \times (TV_{RI}/V_{RI})$ where TV_{RI} = target volume covered by the reference isodose, TV = target volume and V_{RI} = the volume of the reference isodose. 95% isodose was selected for the reference isodose.

Table 4. Summary of the maximum and mean doses to non-target structures: mean value (range)

	3DCRT	IMRT	Difference	*p* value
Cochlea				
D_{max} (%)	99.8 (93.70–102.8)	91.9 (74.10–102.3)	–7.9	< 0.001
D_{mean} (%)	94.9 (79.10–100.4)	72.6 (55.40–79.70)	–22.3	< 0.001
Pituitary gland				
D_{max} (%)	100.4 (98.30–101.7)	101.5 (98.90–102.9)	+1.1	0.003
D_{mean} (%)	99.9 (97.40–101.3)	98.8 (87.00–101.6)	–1.1	0.256
Optic nerve				
D_{max} (%)	99.9 (94.80–101.5)	101.2 (93.30–103.6)	+1.3	0.004
D_{mean} (%)	70.7 (30.90–96.10)	65.8 (25.60–94.70)	–4.9	0.039
Chiasm				
D_{max} (%)	100.5 (98.70–101.8)	101.7 (99.50–103.1)	+1.2	0.002
D_{mean} (%)	100.2 (98.30–101.4)	100.8 (97.70–102.5)	+0.6	0.077
Lens				
D_{max} (%)	5.7 (2.40–20.1)	7.0 (2.3–14.1)	+1.2	0.266
D_{mean} (%)	3.8 (2.2–9.9)	5.2 (2.10–12.3)	+1.4	0.021

Abbreviations: 3DCRT = four-field coplanar three-dimensional conformal radiotherapy; IMRT = seven-field coplanar intensity-modulated radiotherapy; D_{max} = the maximum dose to the structure; D_{mean} = the mean dose to the structure.

Table 5. Published planning studies of intensity-modulated radiotherapy for whole ventricles

	Roberge *et al*. (13)	Raggi *et al*. (14)	Chen *et al*. (20)	Sakanaka
Number of patients	10	5	10	12
Histology	Germinoma	Germinoma	ICGCT	Germinoma
Beam arrangement	non-coplanar	non-coplanar	coplanar	coplanar
Number of fields	7	7	5-10	7
Prescribed dose to WV (Gy)	30	24	25.2-37.5*	24
PTV				
D1% or D_{max} (%)	NA	102-104	NA	104.3
D_{mean} (%)	NA	99.6	NA	102
D95% (%)	NA	> 95	NA	99.9
D99% or D_{min} (%)	NA	> 92	NA	97.7
V100% (%)	NA	NA	NA	93.5
HI (%)	NA	NA	NA	1.17
Normal brain				

Mean dose	Decrease in IMRT	Decrease in IMRT	NA	Decrease in IMRT
low dose irradiated volume	Increase in IMRT	Increase in IMRT	Decrease in IMRT[†]	No significant difference
Conformation number				
3DCRT	NA	NA	NA	0.48
IMRT	NA	NA	NA	0.7
Monitor units				
3DCRT	NA	NA	534[††]	249[§]
IMRT			1038[††]	980[§]

Abbreviations: ICGCT = intracranial germ cell tumor; PTV = planning target volume; D1% = the dose that covers 1% of the structure volume; D_{max} = the maximum dose to the structure, D_{mean} = the mean dose to the structure; D95% = the dose that covers 95% of the structure volume; D99% = the dose that covers 99% of the structure volume; D_{min} = the minimum dose to the structure; V100% = the percentage of the structure volume receiving the prescribed dose; HI = homogeneity index (D_{max}/D_{min}); normal brain = the brain outside the PTV; IMRT = intensity-modulated radiotherapy; Conformation number = $(TV_{RI}/TV) \times (TV_{RI}/V_{RI})$ where TV_{RI} = target volume covered by the reference

isodose, TV = target volume and VRI = the volume of the reference isodose. 95% isodose was selected for the reference isodose; 3DCRT = three-dimensional conformal radiotherapy; NA = not available.

*The median prescribed dose for WV was 30.6 Gy (range 25.2-37.5 Gy) and the boost for the primary lesion was 16.5 Gy (range 0–23.4 Gy).

†The dose-volume comparisons between 3DCRT and IMRT were based on the summed plan of radiotherapy for WV and the boost for the primary lesion.

††The median value of monitor units to deliver a 1.5 to 2.0-Gy fraction in ten patients.

§The mean value of monitor units to deliver a 2.0-Gy fraction in 12 patients.